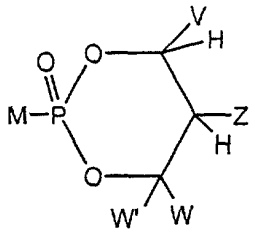
We Claim:

1. A method of enhancing oral bioavailability of a parent drug by administering to an animal a prodrug of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of –CHR^2OH , -$CHR^2OC(O)R^3$, -$CHR^2OC(S)R^3$, -$CHR^2OC(S)OR^3$, -$CHR^2OC(O)SR^3$, -$CHR^2OCO_2R^3$, -OR^2 , -SR^2, -CHR^2N_3, -CH_2aryl, -CH(aryl)OH, -$CH(CH=CR^2_2)OH$, -$CH(C\equiv CR^2)OH$, -R^2 , -NR^2_2, -$OCOR^3$, -OCO_2R^3, -$SCOR^3$, -SCO_2R^3, -$NHCOR^2$, -$NHCO_2R^3$, -CH_2NHaryl, -$(CH_2)_p$-OR^{12}, and -$(CH_2)_p$-SR^{12};

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is -R^2, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

2. The method of claim 1 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

3. The methods of claim 2 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

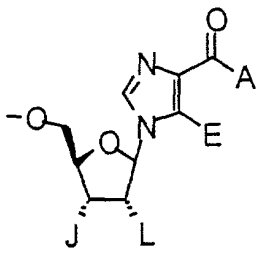
R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl; and

R^{12} is selected from the group consisting of -H, and lower acyl.

4. The method of claim 3 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

5. The method of claim 3 wherein M is a compound of formula II:



II

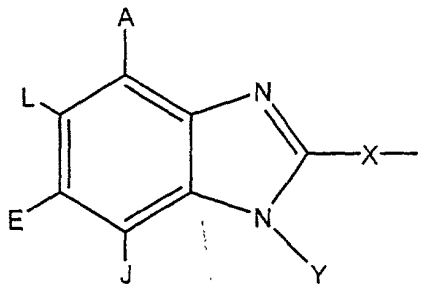
wherein

E is selected from the group consisting of alkyl, amino or halogen;

L and J are independently selected from the group consisting of hydrogen, hydroxy, acyloxy, alkoxycarbonyloxy, or when taken together form a lower cyclic ring containing at least one oxygen; and

A is selected from the group consisting of amino and lower alkylamino; and pharmaceutically acceptable salts thereof.

6. The method of claim 3 wherein M is a compound of formula IV:



wherein:

A, E, and L are selected from the group consisting of $-NR^8_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-COR^{11}$, $-SO_2R^3$, guanidine, amidine, $-NHSO_2R^5$, $-SO_2NR^4_2$, -CN, sulfoxide, perhaloacyl, perhaloalkyl, perhaloalkoxy, C1-C5 alkyl, C2-C5 alkenyl, C2-C5 alkynyl, and lower alicyclic, or together A and L form a cyclic group, or together L and E form a cyclic group, or together E and J form a cyclic group including aryl, cyclic alkyl, and heterocyclic;

J is selected from the group consisting of $-NR^8_2$, $-NO_2$, -H, $-OR^7$, $-SR^7$, $-C(O)NR^4_2$, halo, $-C(O)R^{11}$, -CN, sulfonyl, sulfoxide, perhaloalkyl, hydroxyalkyl, perhaloalkoxy, alkyl,

haloalkyl, aminoalkyl, alkenyl, alkynyl, alicyclic, aryl, and aralkyl, or together with O forms a cyclic group including aryl, cyclic alkyl and heterocyclic alkyl;

X is selected from the group consisting of alkylamino, alkyl(hydroxy), alkyl(carboxyl), alkyl(phosphonate), alkyl, alkenyl, alkynyl, alkyl(sulfonate), aryl, carbonylalkyl, 1,1-dihaloalkyl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alkylaminocarbonyl, alkylcarbonylamino, alicyclic, aralkyl, and alkylaryl, all optionally substituted; or together with O forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

O is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except -H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidentate alkyl;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof; with the provisos that:

a) when X is alkyl or alkene, then A is $-NR^8_2$;

b) X is not alkylamine and alkylaminoalkyl when an alkyl moiety is substituted with phosphonic esters and acids; and

c) A, L, E, J, O, and X together may only form 0-2 cyclic groups.

7. The method of claim 1 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is useful for the treatment of diseases of the liver or metabolic diseases where the liver is responsible for the overproduction of a biochemical end product.

8. The method of claim 7 wherein said disease of the liver is selected from the group consisting of hepatitis, cancer, fibrosis, malaria, gallstones, and chronic cholecystalithiasis.

9. The methods of claim 8 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is an antiviral or anticancer agent.

10. The method of claim 7 wherein said metabolic disease is selected from the group consisting of diabetes, atherosclerosis, and obesity.

11. The method of claim 7 wherein said biochemical end product is selected from the group consisting of glucose, cholesterol, fatty acids, and triglycerides.

12. The method of claim 11 wherein MPO_3^{2-} is an AMP activated protein kinase activator.

13. The method of claim 1 wherein M -PO_3^{2-} is a compound that inhibits human liver FBPase.

14. The method of claim 13 wherein said compound inhibits human liver FBPase with an IC_{50} of less than 10 μM.

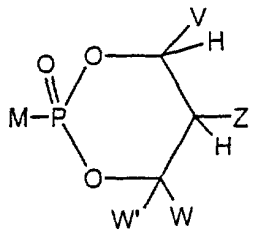
15. The method of claim 1 wherein said oral bioavailability is at least 5%.

16. The method of claim 15 wherein said oral bioavailability is at least 10%.

17. The method of claim 15 wherein said oral bioavailability is enhanced by 50% compared to the parent drug administered orally.

18. The method of claim 16 wherein said oral bioavailability is enhanced by at least 100%.

19. A method of delivering a biologically active drug to an animal for a sustained period using compounds of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

20. The method of claim 19 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

21. The methods of claim 20 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

22. The method of claim 21 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

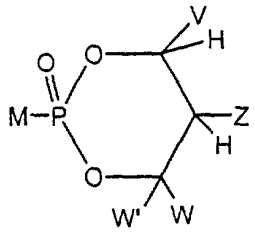
23. The method of claim 19 whereby therapeutic levels of said drug are maintained for at least one hour longer than the levels achieved by oral administration of the bispivaloyloxymethyl (bis-POM) ester.

24. The method of claim 19 whereby therapeutic levels of said FBPase inhibitors are maintained for at least one hour longer after systemic administration relative to an equivalent molar amount of the parent compound administered by the same route.

25. The method of claim 19 wherein MPO_3^{2-} is an FBPase inhibitor.

26. The method of claim 19 wherein MH or MPO_3^{2-} is an antiviral or anticancer agent.

27. A method of delivering a biologically active drug to an animal with greater selectivity for the liver using compounds of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and

aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

28. The method of claim 27 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

29. The methods of claim 28 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, $-CH$(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

30. The method of claim 29 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene

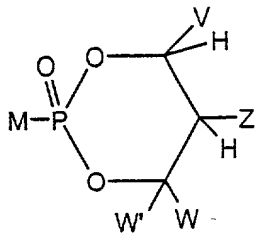
PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

31. The method of claim 27 whereby the ratio of a parent drug or a drug metabolite concentration in the liver over a parent drug or a drug metabolite concentration in the plasma is two times greater compared to administration of a parent drug.

32. The method of claim 31 wherein the liver specificity has increased relative to administration of M-PO_3^{2-}.

33. The method of claim 27 wherein said biologically active drug is a triphosphate generated in the liver.

34. A method of increasing the therapeutic index of a drug by administering to an animal compounds of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

35. The method of claim 34 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

36. The methods of claim 35 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

37. The method of claim 36 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9

(arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

38. The method of claim 34 wherein extrahepatic toxicity is reduced.

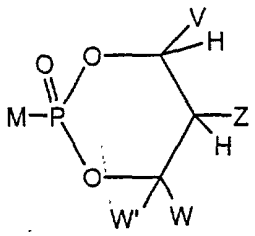
39. The method of claim 38 wherein $M\text{-}PO_3^{2-}$ is excreted by the kidney.

40. The method of claim 38 wherein the M is selected from the group consisting of PMEA, PMEADAP, HPMPS, HPMPA, FPMPA, and PMPA.

41. The method of claim 38 wherein the gastrointestinal toxicity is reduced.

42. The method of claim 38 wherein central or peripheral nervous system toxicity is reduced.

43. A method of bypassing drug resistance by administering to an animal compounds



of formula I:

I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

44. The method of claim 43 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

45. The methods of claim 44 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

46. The method of claim 45 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC,

araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, *tiazofurin*, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

47. The method of claim 43 wherein said resistance arises from decreased cellular production of $M\text{-}PO_3^{2-}$.

48. The method of claim 43 wherein said compound is an anticancer or antiviral agent.

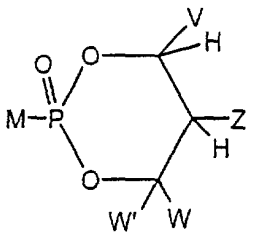
49. The method of claim 48 wherein M is 5-fluoro-2'-deoxyuridine.

50. The method of claim 48 wherein said resistance is to an antiviral agent selected from the group consisting of araA, AZT, d4T, 3TC, ribavirin, 5 fluoro-2'deoxyuridine, FMAU, DAPD, FTC, 5-yl-carbocyclic 2'deoxyguanosine, Cyclobut G, dFdC, araC, IDU, FaraA, ACV, GCV, and penciclovir.

51. The method of claim 48 wherein the resistance or lack of antihepatitis activity is due to a deficiency in thymidine kinase and said antiviral agent is selected from the group consisting of AZT, d4T, and ACV.

52. The method of claim 48 wherein said anticancer agent is selected from the group consisting of dFdC, araC, F-araA, and CdA.

53. A method of treating cancer by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$,

$-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

54. The method of claim 53 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

55. The methods of claim 54 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2aryl$, $-CH(aryl)OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$,

$-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

56. The method of claim 55 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

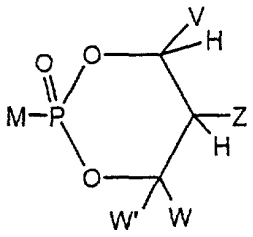
57. The method of claim 53 wherein the active drug is the triphosphate of M-H.

58. The method of claim 53 wherein the active drug is the monophosphate of M-H.

59. The method of claim 53 wherein MH is selected from the group consisting of dFdC, araC, FaraA, CdA, 5-fluoro 2'deoxyuridine, GCV, tiazofurin, IDU, 5,6 dihydro-5-azacytidine, 5-azacytidine, and 5-aza 2'deoxycytidine.

60. The method of claim 59 wherein MH is selected from the group consisting of dFdC, araC, FaraA, CdA, and 5-fluoro 2'deoxyuridine.

61. A method of treating viral infections by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

62. The method of claim 61 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom.

63. The methods of claim 62 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

64. The method of claim 63 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

65. The method of claim 61 wherein said viral infection is hepatitis.

66. The method of claim 65 wherein said hepatitis is hepatitis B.

67. The methods of claim 61 wherein viral kinases produce M-PO_3^{2-}.

68. The method of claim 61 wherein said viral infection is hepatitis and said viral kinases are kinases from viruses other than the hepatitis viruses.

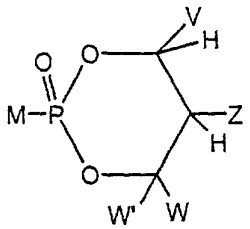
69. The method of claim 61 wherein the active drug is the triphosphate of M-H.

70. The method of claim 61 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, FIAU, FIAC, L-FMAU, TFT, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl carbocyclic 2'deoxyguanosine, cytallene, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, araT, ACV, GCV, penciclovir, PMEA, PMEDAP, HPMPC, HPMPA, PMPA, and foscarnet.

71. The method of claim 70 wherein MH is selected from the group consisting of 3TC, penciclovir, FMAU, DAPD, FTC, Cyclobut G, ACV, GCV, PMEA, HPMPA, 5-yl-carbocyclic 2'deoxyguanosine, and ribavirin.

72. The method of claim 71 wherein MH is selected from the group consisting of dFdC, araC, FaraA, CdA, 5-fluoro 2'deoxyuridine, GCV, tiazofurin, IDU, 5,6 dihydro-5-azacytidine, 5-azacytidine, and 5-aza 2'deoxycytidine.

73. A method of treating liver fibrosis by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

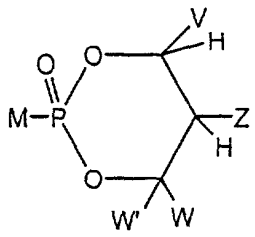
R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

74. A method of treating hyperlipidemia by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

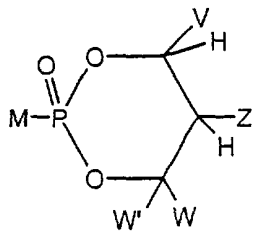
R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

75. The method of claim 74 wherein the hyperlipidemia agent is a squalene synthase inhibitor.

76. A method of treating parasitic infections by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

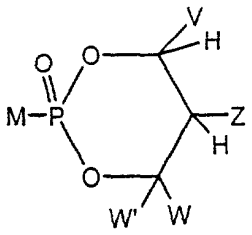
R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

77. A method of delivering diagnostic imaging agents to the liver comprising administration to an animal of compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

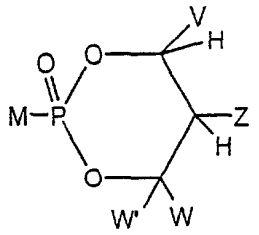
M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

78. The method of claim 77 wherein MH is IDU.

79. A method of making a prodrug of a compound drug having a $-PO_3^{2-}$ moiety comprising,

a) transforming said phosph(on)ate into a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$,

$-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

80. The method of claim 79 further comprising,

a) converting $M-PO_3^{2-}$ to a compound $M-P(O)L"_2$ wherein L" is a leaving group selected from the group consisting of halogen; and

b) reacting $M-P(O)L"_2$ with HO-CH(V)CH(Z)CH(Z)-CW(W')-OH.

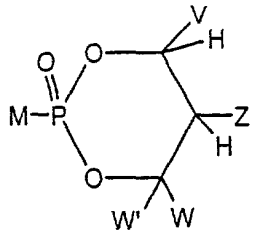
81. The method of claim 80 wherein HO-CH(V)CH(Z)-CW(W')-OH is a single stereoisomer.

82. The method of claim 81 further comprising isolating a single diastereomer.

83. A method of making a prodrug of formula I by

a) converting a hydroxyl or amino or MH to a phosph(oramid)ite by reaction with L-P(-OCH(V)CH(Z)-CW(W')O-) wherein L selected from the group consisting of NR^1_2, and halogen;

b) transforming said phosph(oramid)ite into a compound of formula I by reaction with an oxidizing agent, wherein



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$,

$-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

84. The method of claim 83 wherein L-P(-OCH(V)CH(Z)-CW(W')O-) is a single stereoisomer.

85. The method of claim 83 further comprising isolating a single diastereomer of said phosph(oramid)ite, M-P(-OCH(V)CH(Z)-CWW-O-).

86. The method of claim 84 wherein said oxidizing agent produces a major stereoisomer at the phosphorus in a ratio of at least 3:1.

87. The method of making a prodrug of formula I comprising converting a hydroxyl or an amino to a phosphate or phosphoramidate, respectively, by reaction with L'-P(O)(-OCH(V)CH(Z)-CW(W')O-) wherein L' is a leaving group selected from the group consisting of $-NR_2$, aryloxy, and halogen.

88. The method of claim 87 wherein L'-P(O)(-OCH(V)CH(Z)-CW(W')O-) is a single stereoisomer.

89. The method of claim 88 wherein said stereoisomer is generated using a chiral diol.

90. The method of claim 79 further comprising the step of reacting $M\text{-}PO_3^{2-}$ with a coupling reagent and HO-CH(V)CH(Z)CWW'OH.

91. The method of claim 90 wherein said coupling reagent is selected from the group consisting of DCC, EDCI, CDI, and di-isopropylcarbodiimide.

92. The method of claim 91, wherein HO-CH(V)CH(Z)CWW'OH is a single stereoisomer.

93. A compound,

$R^1{}_2N\text{-}P\text{-}(\text{-}OCH(V)CH(Z)\text{-}CW(W')O\text{-})$

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

and pharmaceutically acceptable prodrugs and salts thereof.

each R^1 is independently selected from the group consisting of alkyl, aryl, and aralkyl;

or together R^1 and R^1 form a cyclic group, optionally containing a heteroatom;

with the proviso that both R^1 groups are not benzyl or ethyl at the same time.

94. A compound $\overline{R^1}_2\overline{N}\text{-}\overline{P}(O)(\text{-}OCH(V)CH(Z)\text{-}CW(W')O\text{-})$

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

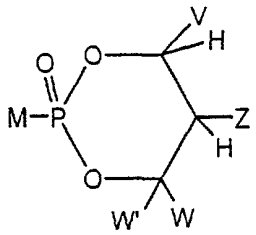
R^{12} is selected from the group consisting of -H, and lower acyl;

each R^1 is independently selected from the group consisting of alkyl, aryl, and aralkyl;

or together R^1 and R^1 form a cyclic group, optionally containing a heteroatom;

with the proviso that both R^1 groups are not benzyl or ethyl at the same time.

95. A compound of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both O groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma position to the O attached to the phosphorus;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$,

$-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, or $P_3O_9^{4-}$ is a biologically active agent and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom with the proviso that $M-PO_3^{2-}$ is not an FBPase inhibitor;

and pharmaceutically acceptable prodrugs and salts thereof.

96. The compounds of claim 95 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, and $MP_3O_9^{4-}$ is selected from the group consisting of an antiviral, anticancer, anti-fibrotic, antihyperlipidemic, anti-diabetic, and antiparasitic agents.

97. The compound of claim 95 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, and $MP_3O_9^{4-}$ is selected from the group consisting of metalloprotease inhibitor, and TS inhibitor.

98. The method of claim 3 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

99. The compounds of claim 96 wherein MH is selected from the group consisting of ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

100. The compounds of claim 95 wherein M is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.

101. The compounds of claim 95 wherein M-PO_3^{2-} is selected from the group consisting of phospohonoformic acid, and phosphonoacetic acid.

102. The compounds of claim 95 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

103. The compounds of claim 102 wherein V is selected from the group consisting of aryl, substitued aryl, heteroaryl, substituted heteroaryl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, that is fused to an aryl group attached at the beta and gamma position to the O attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form a cyclic substituted group containing 6 carbon atoms and mono-substituted with a substituent selected from the group consisting of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an O attached to the phosphorus.

104. The compounds of claim 103 wherein V is selected from the group consisting of aryl, substitued aryl, heteroaryl, and substituted heteroaryl.

105. The compounds of claim 104 wherein Z, W, and W' are H.

106. The compounds of claim 106 wherein V is selected from the group consisiting of aryl and substituted aryl.

107. The compounds of claim 106 wherein V is selected from the group consisting of phenyl, and substituted phenyl.

108. The compounds of claim 107 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, and 3-bromophenyl.

109. The compounds of claim 108 wherein V is selected from the group consisting of heteroaryl and substituted heteroaryl.

110. The compounds of claim 109 wherein V is 4-pyridyl.

111. The compounds of claim 103 wherein together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma positions to the O attached to phosphorus.

112. The compounds of claim 111 wherein said aryl group is an optionally substituted monocyclic aryl group and the connection between Z and the gamma position of the aryl group is selected from the group consisting of O, CH_2, CH_2 CH_2, OCH_2 or CH_2O.

113. The compounds of claim 103 wherein together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and mono-substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an O attached to the phosphorus.

114. The compounds of claim 113 wherein together V and W form a cyclic group selected from the group consisting of - CH_2-CH(OH)- CH_2-, -$CH_2CH(OCOR^3)$-CH_2-, and -$CH_2CH(OCO_2R^3)$-CH_2-.

115. The compounds of claim 102 wherein V is -H, and Z is selected from the group consisting of –CHR^2OH , -CHR^2OCOR^3, and -$CHR^2OCO_2R^3$.

116. The compounds of claim 104 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 4-pyridyl;

Z is selected from the group consisting of –OR^2, -SR^2, -CHR^2N_3, -R^2 , -NR^2_2, -$OCOR^2$, -OCO_2R^3, -$SCOR^3$, -SCO_2R^3, -$NHCOR^2$, -$NHCO_2R^3$, -CH_2NHaryl, -$(CH_2)_p$-OR^{12}, and -$(CH_2)_p$-SR^{12}.

117. The compounds of claim 116 wherein Z is selected from the group consisting of $-OR^2$, $-R^2$, $-OCOR^2$, $-OCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and, $-(CH_2)_p-SR^{12}$.

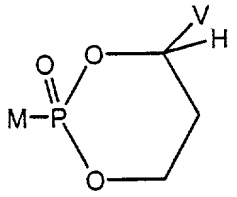
118. The compounds of claim 117 wherein Z is selected from the group consisting of $-OR^2$, -H, $-OCOR^2$, $-OCO_2R^3$, and $-NHCOR^2$.

119. The compounds of claim 104 wherein W and W' are independently selected from the group consisting of H, R^3, aryl, substituted aryl, heteroaryl, and substituted aryl.

120. The compounds of claim 119 wherein W and W' are the same group.

121. The compounds of claim 120 wherein W and W' are H, or $-CH_3$.

122. The compounds of claim 104 wherein said prodrug is a compound of formula VI:



VI

wherein

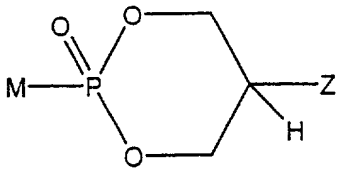
V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

123. The compounds of claim 122 wherein M is attached to phosphorus via an oxygen or nitrogen atom.

124. The compounds of claim 122 wherein V is selected from the group consisting of phenyl and substituted phenyl.

125. The compounds of claim 123 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 4-pyridyl.

126. The compounds of claim 102 wherein said prodrug is a compound of formula VII:



VII

wherein

Z is selected from the group consisting of:

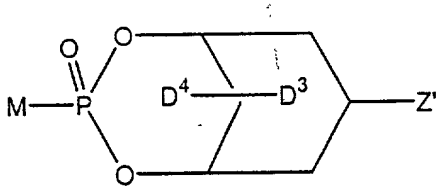
-CHR^2OH, -$CHR^2OC(O)R^3$, -$CHR^2OC(S)R^3$, -$CHR^2OCO_2R^3$, -$CHR^2OC(O)SR^3$, -$CHR^2OC(S)OR^3$, -SR^2, and -CH_2aryl.

127. The compounds of claim 126 wherein M is attached to the phosphorus via a nitrogen or oxygen atom.

128. The compounds of claim 127 wherein Z is selected from the group consisting of -CHR^2OH, -$CHR^2OC(O)R^3$, and -$CHR^2OCO_2R^3$.

129. The compounds of claim 128 wherein R^2 is -H.

130. The compounds of claim 102 wherein said prodrug is a compound of formula VIII:



VIII

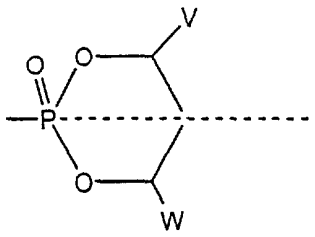
wherein

Z' is selected from the group consisting of -OH, -$OC(O)R^3$, -OCO_2R^3, and -$OC(O)S\ R^3$;

D^3 and D^4 are independently selected from the group consisting of -H, alkyl, -OH, and -$OC(O)R^3$.

131. The compounds of claim 130 wherein D^3 and D^4 are -H.

132. The compounds of claim 102 wherein W' and Z are -H, W and V are both the same aryl, substituted aryl, heteroaryl, or substituted heteroaryl such that the phosphonate prodrug moiety:



has a plane of symmetry.

133. The compounds of claim 102 wherein W and W' are H, V is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, and Z is selected from the group consisting of -H, OR^2, and $-NHCOR^2$.

134. The compounds of claim 133 wherein Z is -H.

135. The compounds of claim 102 wherein phosphorus is attached to an oxygen in a primary hydroxyl group on M.

136. The compounds of claim 135 wherein V is selected from the group consisting of phenyl or substituted phenyl.

137. The compounds of claim 136 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, and 3-bromophenyl.

138. The compounds of claim 135 wherein V is an optionally substituted monocyclic heteroaryl containing at least one nitrogen atom.

139. The compounds of claim 138 wherein V is 4-pyridyl.

140. The compounds of claims 122, 126, or 130 wherein MH is selected from the group consisting of araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, and AICAR.

141. The compounds of claims 122, 126, or 130 wherein MH is selected from the group consisting of ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

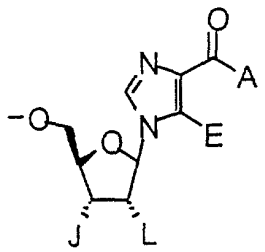
142. The compounds of claims 122, 126, or 130 wherein M is attached to the phosphorus via a carbon atom.

143. The compounds of claims 122, 126, or 130 wherein MPO_3^{2-} is selected from the group consisting of phosphonoformic acid, and phosphonoacetic acid.

144. The compounds of claims 122, 126, or 130 wherein MH is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.

145. The compounds of claim 122 wherein V is selected from the group consisting of phenyl substituted with 1-3 halogens and 4-pyridyl, and MH is selected from the group consisting of araA, AZT, d4T, 3TC, ribavirin, 5 fluoro-2'deoxyuridine, FMAU, DAPD, FTC, 5-yl-carbocyclic 2'deoxyguanosine, Cyclobut G, dFdC, araC, IDU, FaraA, ACV, GCV, and penciclovir, PMEA, HPMPC, and HPMPA.

146. The compounds of claims 122, 126, or 130 wherein M is selected from the group consisitng of:



II

wherein

E is selected from the group consisting of alkyl, amino or halogen;

L and J are independently selected from the group consisting of hydrogen, hydroxy, acyloxy, alkoxycarbonyloxy, or when taken together form a lower cyclic ring containing at least one oxygen; and

A is selected from the group consisting of amino and lower alkylamino; and pharmaceutically acceptable prodrugs and salts thereof.

147. The compounds of claims 95 wherein MH is an acyclic nucleoside.

148. The compounds of claim 147 wherein MH is selected from the group consisting of ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

149. The compounds of claim 148 wherein MH is selected from the group consisting of ACV, GCV, and penciclovir.

150. The compounds of claim 95 wherein MH is a dideoxy nucleoside.

151. The compounds of claim 150 wherein MH is selected from the group consisting of AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L d4C, L-Fd4C, d4C, and ddAPR.

152. The compounds of claim 151 wherein MH is selected from the group consisting of AZT, d4T, ddI, and ddC.

153. The compounds of claim 95 wherein MH is an arabinofuranosyl nucleoside.

154. The compounds of claim 153 wherein MH is selected from the group consisting of araA, araT, 5-propynyl-1-arabinosyluracil, araC, FaraA, 9-(arabinofuranosyl)-2,6 diaminopurine, and 9-(arabinofuranosyl)guanine.

155. The compounds of claim 154 wherein MH is selected from the group consisting of araA, araC, and FaraA.

156. The compounds of claim 95 wherein MH is a carbocyclic nucleoside.

157. The compounds of claim 156 wherein MH is selected from the group consisting of 5-yl-carbocyclic 2'deoxyguanosine, CDG, cyclobut A, cyclobut G, and BHCG.

158. The compounds of claim 157 wherein MH is selected from the group consisting of 5-yl-carbocyclic 2'deoxyguanosine, and cyclobut G.

159. The compounds of claim 95 wherein MH is a fluoro sugar nucleoside.

160. The compounds of claim 159 wherein MH is selected from the group consisting of FLT, FLG, FIAC, FIAU, FMAU, FEAU, dFdC, 9-(2'-deoxy-2'fluororibofuranosyl) 2,6-diaminopurine, and 9-(2'-deoxy 2'fluororibofuranosyl)guanine.

161. The compounds of claim 160 wherein MH is selected from the group consisting of L-FMAU, and dFdC.

162. The compounds of claim 95 wherein MH is a dioxolane nucleoside.

163. The compounds of claim 162 wherein MH is selected from the group consisting of DAPD, DXG, and FDOC.

164. The compounds of claim 163 wherein MH is selected from the group consisting of DAPD.

165. The compounds of claim 95 wherein MH is an L-nucleoside.

166. The compounds of claim 165 wherein MH is selected from the group consisting of L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC, FTC, and L-FMAU.

167. The compounds of claim 166 wherein MH is selected from the group consisting of 3TC, FTC, and L-FMAU.